

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Previously Presented) A method of identifying a compound that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

(a) contacting a member of a library of compounds with a cell containing a first nucleic acid sequence and a second nucleic acid sequence, wherein the first nucleic acid sequence comprises a regulatory element operably linked to a reporter gene and the second nucleic acid sequence comprises a nucleotide sequence with a premature stop codon that encodes a regulatory protein that binds to the regulatory element of the first nucleic acid sequence and regulates the expression of the reporter gene; and

(b) detecting the expression of the reporter gene, wherein a compound that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or the presence of a negative control.

2. (Currently Amended) A method of identifying a compound that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

(a) contacting a member of a library of compounds with a cell containing a first nucleic acid sequence, a second nucleic acid sequence and a third nucleic acid sequence, wherein (i) the first nucleic acid sequence comprises a nucleotide sequence encoding a first fusion protein comprising a DNA binding domain and a first protein, the nucleotide sequence encoding of the first protein containing comprising a premature stop codon, (ii) the second nucleic acid sequence comprises a nucleotide sequence encoding a second fusion protein comprising an activation domain and a second protein, the second protein interacting with the first protein to produce a regulatory protein, and (iii) the third nucleic acid sequence comprises a regulatory element operably linked to a reporter gene, the expression of the reporter gene being regulated by the binding of the regulatory protein to the regulatory element; and

(b) detecting the expression of the reporter gene, wherein a compound that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or the presence of a negative control.

3. (Currently Amended) A method of identifying a compound that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

(a) contacting a member of a library of compounds with a cell containing a first nucleic acid sequence, a second nucleic acid sequence and a third nucleic acid sequence, wherein (i) the first nucleic acid sequence comprises a nucleotide sequence encoding a first fusion protein comprising a DNA binding domain and a first protein, (ii) the second nucleic acid sequence comprises a nucleotide sequence encoding a second fusion protein comprising an activation domain and a second protein, the nucleotide sequence encoding of the second protein containing comprising a premature stop codon and the second protein interacting with the first protein to produce a regulatory protein, and (iii) the third nucleic acid sequence comprises a regulatory element operably linked to a reporter gene, the expression of the reporter gene being regulated by the binding of the regulatory protein to the regulatory element; and

(b) detecting the expression of the reporter gene, wherein a compound that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or the presence of a negative control.

4. (Currently Amended) A method for identifying a compound that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

(a) contacting a member of a library of compounds with a cell-free translation mixture and a nucleic acid sequence comprising a regulatory element operably linked to a reporter gene, wherein the reporter gene contains comprises a premature stop codon and the cell-free translation mixture is isolated from cells that have been incubated ~~at about 0°C to about 10°C on ice at least 12 hours~~; and

(b) detecting the expression of the reporter gene, wherein a compound that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or the presence of a negative control.

5. (Currently Amended) A method for identifying a compound that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

(a) contacting a member of a library of compounds with a cell-free translation mixture and a nucleic acid sequence comprising a regulatory element operably linked to a reporter gene, wherein the reporter gene ~~contains~~ comprises a premature stop codon and the cell-free translation mixture is a ~~S10 to S30~~ S12 cell-free extract; and

(b) detecting the expression of the reporter gene, wherein a compound that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the expression of the reporter gene in the presence of the compound is altered relative to the expression of the reporter gene in the absence of the compound or the presence of a negative control.

6. (Previously Presented) The method of claim 4, wherein the cell-free translation mixture is a S10 to S30 cell-free extract.

7. (Canceled)

8. (Previously Presented) The method of claim 6, wherein the cell-free translation mixture is a S12 cell-free extract.

9. – 10. (Canceled)

11. (Previously Presented) The method of claim 1, 2, 3, 4 or 5, wherein the method further comprises determining the structure of the compound that ~~suppresses~~ modulates premature translation termination or nonsense-mediated mRNA decay.

12. (Canceled)

13. (Currently Amended) The method of claim 1, 2, 3, 4, or 5, 9 or 10, wherein the reporter gene is firefly luciferase, renilla luciferase, click beetle luciferase, green fluorescent protein, yellow fluorescent protein, red fluorescent protein, cyan fluorescent protein, blue fluorescent protein, beta galactosidase, beta glucuronidase, beta lactamase, chloramphenicol acetyltransferase, or alkaline phosphatase.

14. (Currently Amended) The method of claim 1, 2, or 3 or 9, wherein the cell is selected from the group consisting of 293T, HeLa, MCF7, Wi-38, SkBr3, Jurkat, CEM, THP1, 3T3, and Raw264.7 cells.

15. (Currently Amended) The method of claim 4, or 5 or 10, wherein the cell-free translation mixture is a cell-free extract from 293T, HeLa, MCF7, Wi-38, SkBr3, Jurkat, CEM, THP1, 3T3, or Raw264.7 cells.

16. (Currently Amended) The method of claim 1, 2, 3, 4, or 5, 9 or 10, wherein the compound is selected from a combinatorial library of compounds comprising peptoids; random biooligomers; diversomers such as hydantoins, benzodiazepines and dipeptides; vinylogous polypeptides; nonpeptidal peptidomimetics; oligocarbamates; peptidyl phosphonates; peptide nucleic acid libraries; antibody libraries; carbohydrate libraries; and small organic molecule libraries.

17. (Previously Presented) The method of claim 16, wherein the small organic molecule libraries are libraries of benzodiazepines, isoprenoids, thiazolidinones, metathiazanones, pyrrolidines, morpholino compounds, or diazepindiones.

18. (Currently Amended) The method of claim 1, 2, 3, 4, or 5, 9 or 10, wherein the premature stop codon UAG or UGA.

19. (Currently Amended) The method of claim 1, 2, 3, 4, or 5, 9 or 10, wherein the premature stop codon context is UAGA, UAGC, UAGG, UAGU, UGAA, UGAC, UGAG or UGAU.

20. (New) The method of claim 4, wherein the cells have been incubated on ice for at least 24 hours.

21. (New) The method of claim 4, wherein the cell-free translation mixture is a S5 to S25 cell-free extract.

22. (New) The method of claim 6, wherein the cell-free translation mixture is a S10 cell-free extract.

23. (New) The method of claim 4, wherein the reporter gene comprises 2 premature stop codons.

24. (New) The method of claim 5, wherein the reporter gene comprises 2 premature stop codons.

25. (New) The method of claim 1, 2 or 3, wherein the compound is a small molecule.

26. (New) The method of claim 4 or 5, wherein the compound is a small molecule.

27. (New) The method of claim 1, 2 or 3, wherein the compound reduces or suppresses premature translation termination or nonsense-mediated mRNA decay.

28. (New) The method of claim 4 or 5, wherein the compound reduces or suppresses premature translation termination or nonsense-mediated mRNA decay.